

REMARKS

A petition for a one-month retroactive extension of time and fee authorization accompanies this amendment.

This is in response the Office Action dated March 27, 2002 in the subject application. Claims 36-59 were under consideration for the purposes of this action. Applicant has canceled the previously pending claims 36-59, and submits new claims 60-83 which are directed to a more specific aspect of the subject matter. These new claims contain no new matter because they recite the method of A β reduction as previously claimed in claims 47-54 and 56, and originally filed as claims 7-17, and 19-28.

The newly presented claims have been amended solely to expedite prosecution of this application and in no way should be deemed as an acquiescence to the rejections of any other claims. Applicant reserves the right to prosecute any remaining subject matter in a continuing application.

Applicant wishes to thank the Examiner for granting the telephonic interview on March 13, 2002 with applicant's attorney and the consequent withdrawal of the rejection under 35 USC 102(b) citing Simons et al.

Applicant also gratefully acknowledges the withdrawal of the objection of claims 9-16 under 37 CFR 1.75(c) and withdrawal of the rejection of claims 1-28 and 33 under 35 USC § 112, second paragraph.

Claims 36-59 remain rejected under 35 USC 103(a) as being unpatentable over Scolnick (WO 95/06740) in view of Sabbaugh et al. and May. Applicant respectfully traverses. A rejection under 35 USC 103(a) requires a teaching or suggestion of the claimed invention be founded in the prior art. The subject invention, as now claimed in

newly presented claims 60-83 is directed to a method of lowering beta amyloid (A β) levels in a mammal. Nowhere in the cited references, taken alone or in combination, is there a teaching or suggestion of reducing A β levels by administering an HMG CoA reductase inhibitor.

Scolnick, the primary reference relied on in the instant Office Action, fails to teach or suggest the claimed invention because there is no mention of A β or any effect on A β by the administration of an HMG-CoA reductase inhibitor. Scolnick describes that administering an HMG-CoA reductase inhibitor lowers a variant protein, namely, Apolipoprotein E isoform 4 (ApoE 4). See Scolnick p. 9 line 32 - p. 10 line 11. The discussion provided by the Scolnick reference of reducing ApoE 4 levels is completely inapposite to the claimed invention, i.e., reduction of A β because ApoE 4 is known to be completely different from A β in its structure, function, and synthesis. These differences between Apo E 4 and A β , as well as their consequent physiological effects caused by their increased or decreased levels, are more fully explained in the accompanying Declaration Under 37 CFR § 1.132 by Dr. Edward Cullen.

Although Scolnick *speculates* that reduction of ApoE 4 may occur in the brain (p.10, lines 30-31), and that such reduction in the brain may be useful in the treatment of Alzheimer's Disease, it is now known that if ApoE 4 were involved in the pathology of Alzheimer's Disease, any reduction of ApoE 4 would be expected to increase that pathology rather than provide beneficial treatment. This is confirmed in the accompanying expert Declaration of Dr. Cullen which refutes the conclusion taught by Scolnick that the reduction of ApoE 4 would reduce symptoms of Alzheimer's Disease.

Dr. Cullen's statement are based on the current knowledge of lipoprotein biochemistry and genetics, which has significantly advanced since the 1994 publication of Scolnick.

Now that it is known that the reducing of the level of a variant gene product which already has reduced function, such as ApoE 4, will increase the pathology resulting from that reduced activity, the method described by Scolnick, i.e., lowering the reduced- activity protein ApoE 4, would in fact teach away from using an HMG-CoA reductase inhibitor to treat Alzheimer's Disease. A person of ordinary skill in the art, looking at the information provided by Scolnick, and having the current knowledge that ApoE 4 reduction increases any pathology relating to ApoE 4 would conclude that administration of an HMG-CoA reductase inhibitor would be contraindicated for Alzheimer's Disease. Thus, in view of this teaching away, and the contradistinction of the Scolnick teaching outlined by Dr. Cullen, the reference of Scolnick is deficient for teaching or suggesting a method for reducing A β or treating Alzheimer's Disease as claimed in the subject application.

The secondary references, Sabbaugh et al. and May, which are cited in combination with Scolnick for the purpose of classifying Alzheimer's Disease as an APP processing disorder, fail to cure the deficiency of the Scolnick reference because ApoE 4 is not involved in APP processing. Notably, the subject invention, as now claimed, does not generally concern the treatment of APP processing disorders. Instead, the current claims are specifically directed to using an HMG-CoA reductase inhibitor to reduce levels of A β , which the secondary references (taken alone, or in combination with Scolnick) fail to teach or suggest. Therefore, even in combination, the cited references fail to teach or suggest the currently claimed invention.

Furthermore, in order to properly apply a rejection under 35 USC 103(a) with a combination of references, there must be some motivation to combine those references. Here, Scolnick teaches HMG-CoA reductase inhibitors for the treatment of Alzheimer's Disease by reducing levels of ApoE 4. This is now known to be completely incorrect because ApoE 4 reduction would not be an effective way to treat Alzheimer's Disease (see Cullen Declaration, attached). Scolnick does not in any way address reduction of A β . There would be no motivation to combine a reference describing a method of treatment involving ApoE 4, such as Scolnick, with any reference that relates to the completely different peptide, A β , such as Sabbaugh et al. and May.

Conversely, a person of ordinary skill in the art reviewing the references of Sabbaugh et al. and May (which describe the possible involvement of APP processing with Alzheimer's Disease) would not be motivated to look to a reference such as Scolnick, which does not concern APP processing. Therefore, applicant believes that the only motivation to combine these unrelated references is provided by the subject application itself. Hindsight reconstruction of the prior art, using the application itself as a basis to piece together an obviousness rejection is improper. The references relied upon for the obviousness rejection against the subject invention do not, themselves, provide the requisite motivation to combine and are only combined using the subject application as a basis for piecing together the elements of HMG-CoA reductase inhibitors, A β , and Alzheimer's Disease as now claimed. Applicant maintains that, in the absence of a motivation to combine the cited references, the instant obviousness rejection must fall.

Even assuming *arguendo* that the references are properly combined, the absence of a teaching or suggestion founded in the prior art of the claimed subject matter, as

stated above, is further support that an obviousness rejection based on the cited references in combination cannot stand. Applicant therefore respectfully requests that the rejection of claims under 35 USC 103(a) as set forth in the Office Action be reconsidered and withdrawn.

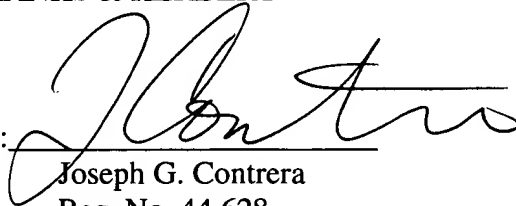
Based upon the foregoing amendments and representations, applicants submit that the rejection of the claims in the above-identified application have been overcome and should be withdrawn. Applicant believes the newly presented claims are in condition for allowance and respectfully requests reconsideration. Early and favorable action is earnestly solicited.

Applicant invites the Examiner to call the undersigned at the telephone number provided below if a telephonic communication would be deemed to expedite further prosecution of this application.

The Assistant Commissioner is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-0622.

Respectfully submitted,

SHANKS & HERBERT

By: 
Joseph G. Contrera
Reg. No. 44,628

Date: 7/29/02

TransPotomac Plaza
1033 N. Fairfax Street
Suite 306
Alexandria, VA 22314